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BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER

KRUSE, DAVID H

ART UNIT PAPER NUMBER

1638

DATE MAILED: 05/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

08/992,914

Applicant(s)

WATANABE ET AL.

Examiner

David H Kruse

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 February 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4,6,7,9,11-13,15-18,30-36,40,41 and 43-45 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 6 and 43 is/are allowed.
- 6) ☒ Claim(s) 1,4,7,9,11-13,15-18,30-36,40,41,44 and 45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 25 February 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. This Office action is in response to the Amendment and Remarks filed 25 February 2004.
2. The drawings were received on 25 February 2004. These drawings are acceptable to the Examiner.
3. The objection to claims 43 and 44 is withdrawn, the Examiner acknowledges Applicants statement that said claims had been previously amended to independent form.
4. Those rejections not specifically addressed in this Office action are withdrawn in view of Applicant's amendments.
5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 101

6. Claims 9, 12, 13, 17, 18 and 44 remain rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a substantial asserted utility or a well-established utility. This rejection is repeated for the reason of record as set forth in the last Office action mailed 26 August 2003. Applicant's arguments filed 25 February 2004 have been fully considered but they are not persuasive.

Applicant argues that the homologies among RFSS are higher than those homologies between RFSS and SIPs and between RFSS and STSS, and that the skilled artisan could rely on homology to determine whether or not a nucleic acid would actually encode a raffinose synthase enzyme (page 22, 2nd paragraph of the Remarks).

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This argument is not found to be persuasive because Applicant has only established that the enzyme encoded by SEQ ID NO: 1 in fact has raffinose synthase activity. Applicant provides no evidence of any special structural feature of raffinose synthases, specifically plant raffinose synthases, by which one of skill in the art could confidently recognize the function of an encoded protein without empirical evidence.

Applicant argues that RFSS, SIPS and STSS can be easily distinguished from one another based upon a comparison of their amino acid sequences, and that amino acid sequence similarity can be used to assert function (page 23, 2nd paragraph of the Remarks). This argument is not found to be persuasive because a separation in a phylogenetic tree does not irrefutably teach the function in the instant case. The Examiner has reviewed Tables 1 and 2 of the Appendix filed with the instant response. While Table 2 shows a variation of between 50-70% identity among the putative and/or confirmed RFSS enzymes at the amino acid level, and between 34-45% identity between the putative and/or confirmed RFSS enzymes and STSS enzymes at the amino acid level, this does not establish that simply based on sequence similarity that one of skill in the art can assert function. Using the BLAST function of NCBI, the *Stachys affinis* stachyose synthase has 51% sequence identity with the *Pisum sativum* raffinose synthase (Accession No CAD20127) and 50% sequence identity with the *Cucumis sativus* raffinose synthase (Accession No AAD02832). These levels of sequence identity are well within the range of sequence identity among the putative and/or confirmed RFSS enzymes at the amino acid level (NCBI can be found at www.ncbi.nlm.nih.gov, see attached NCBI/BLAST search report).

Claim Rejections - 35 USC § 112

7. Claims 9, 12, 13, 17, 18 and 44 remain rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. This rejection is repeated for the reason of record as set forth in the last Office action mailed 26 August 2003. Applicant's arguments filed 25 February 2004 do not specifically address this rejection (page 23, 3rd paragraph of the Remarks).

8. Claims 1, 4, 7, 9, 11-13, 15-18, 30-36, 40, 41 and 44 remain rejected and new claim 45 is rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is repeated for the reason of record as set forth in the last Office action mailed 26 August 2003. Applicant's arguments filed 25 February 2004 have been fully considered but they are not persuasive.

Applicant argues that the homologies between raffinose synthase enzymes and seed imbibition proteins or stachylose synthases are considerably lower than the homologies among raffinose synthase enzymes, and that one of skill in the art could describe a putative raffinose synthase based upon its sequence similarity with known raffinose synthase enzymes (page 24, 2nd paragraph of the Remarks). This argument is not found to be persuasive for the reasons given supra. Using the BLAST function of

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NCBI, the *Stachys affinis* stachyose synthase has 51% sequence identity with the *Pisum sativum* raffinose synthase (Accession No CAD20127) and 50% sequence identity with the *Cucumis sativus* raffinose synthase (Accession No AAD02832). These levels of sequence identity are well within the range of sequence identity among the putative and/or confirmed RFSS enzymes at the amino acid level (NCBI can be found at www.ncbi.nlm.nih.gov, see attached NCBI/BLAST search report).

Applicant argues that the nucleic acids recited in sections and of claims 1, 30, 32, and 36 are described by: (1) origin of the nucleic acid, (2) the PCR primers utilized to obtain the nucleic acid, the ability of the nucleic acid to hybridize with a known nucleic acid under stringent hybridization conditions, and (4) the ability of the nucleic acid to encode a protein which produces raffinose by combining a D-galactosyl group through an $\alpha(1-6)$ bond with a hydroxyl group attached to the carbon atom at position 6 of a D-glucose residue in a sucrose molecule (page 25, 2nd paragraph of the Remarks). This argument is not found to be persuasive. At claim 1, 30, 32, and 36 sections (i), (j), (k) and (l), the nucleic acids are isolated from other plants, although within the same order, family or genus, as the described nucleic acid, wherein Applicant does not adequately describe the genus of nucleic acids isolated from such orders, families or genera as broadly claimed. See *University of California V. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that

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protein from another organism. The specific species of the laminaceous plant and monocotyledonous plant are only described in part, and do not comprise the complete coding sequence, SEQ ID NO: 5 and SEQ ID NO: 7.

Applicant argues that the instant specification describes a plurality of isolated nucleic acids which encode raffinose synthase and that the USPTO considers that the disclosure of one species within the same genus is sufficient (paragraph spanning pages 26-27 of the Remarks). This argument is not found to be persuasive. Applicant fails to establish that they have in fact described nucleic acids encoding raffinose synthase genes other than that described in SEQ ID NO: 1 and 2. Applicant does not describe what structural characteristics of the claimed genus described said genus such that one of skill in the art would recognize that Applicant was in possession of such a genus of nucleic acids as broadly claimed.

9. Claims 1, 4, 7, 9, 11-13, 15-18, 30-36, 40, 41 and 44 remain rejected and new claim 45 is rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid encoding the amino acid sequence of SEQ ID NO: 2, a chimeric nucleic acid comprising said isolated nucleic acid, a transformant comprising said chimeric nucleic acid, a plasmid comprising said nucleic acid, a host organism either a microorganism or plant comprising said plasmid and a method of metabolic modification of a plant comprising introducing said isolated nucleic acid, does not reasonably provide enablement for an isolated nucleic acid encoding the amino acid sequence of SEQ ID NO: 4, 6 or 8, or an isolated nucleic acid that hybridizes with a complement to said isolated nucleic acid isolated from any

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leguminous, lamiaceous or monocotyledonous plant. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This rejection is repeated for the reason of record as set forth in the last Office action mailed 26 August 2003. Applicant's arguments filed 25 February 2004 have been fully considered but they are not persuasive.

Applicant argues that the homologies between raffinose synthase enzymes and seed imbibition proteins or stachylose synthases are considerably lower than the homologies among raffinose synthase enzymes. Thus, one of skill in the art could predict the function of a nucleic acid based upon its sequence similarity with known raffinose synthase enzymes (page 28, 1st paragraph of the Remarks). This argument is not found to be persuasive. This argument has been essentially and extensively addressed above.

Applicant argues that there is a high level of skill in the art (e.g., a Ph.D. in biochemistry or its equivalent), the specification provides considerable direction and guidance, that all of the methods needed to practice the invention are known, and that it would not cause the skilled artisan undue experimentation to make or use the claimed nucleic acids of the present invention (page 29, 2nd paragraph of the Remarks). This argument is not found to be persuasive. First, Applicant is requiring one of skill in the art to confirm that the nucleic acid taught in SEQ ID NO: 3 does in fact encode a raffinose synthase. Second Applicant is requiring one of skill in the art to isolate the complete coding sequence taught in the partial sequences of SEQ ID NO: 5 (stachys) or

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SEQ ID NO: 7 (corn) and confirm that the coding sequence encodes a raffinose synthase. Third, Applicant is requiring one of skill in the art to isolate other nucleic acid encoding raffinose synthase from other leguminous, laminaceous or monocotyledonous plants without sufficient guidance as to what unique structure of the encoded amino acid sequence defines the claimed genus. These facts have lead the Examiner to the opinion that it would have required undue trial and error experimentation by one of skill in the art at the time of Applicant's invention to make and use the genus of isolated nucleic acids as broadly claimed.

Applicant argues that the instant specification provides PCR primers and a detailed description of how to use them to isolate additional examples of nucleic acids encoding raffinose synthase, and that working examples 6-11 show the use of the PCR primers to perform such isolations. Applicant argues that this disclosure constitutes actual variants within the claimed genus and actual methods that can be used to find the next species within the genus, and that the specification further provides a detailed description of an assay that can be used to determine if the protein encoded by an isolated nucleic acid is in fact a protein which produces raffinose (paragraph spanning pages 29-30 of the Remarks). This argument is not found to be persuasive because, as addressed above, Applicant has not adequately enabled the exemplified nucleic acids other than SEQ ID NO: 1, or a nucleic acid that encodes SEQ ID NO: 2.

Applicant argues that all of the methods need to practice the present invention are readily known by the skilled artisan, that the methods needed to obtain such a nucleic acid include DNA isolation from a leguminous plant, PCR amplification using

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specific primers, and hybridization and that it is uncontestable that all of these techniques are widely utilized such that their use is routine the art (paragraph spanning pages 30-31 of the Remarks). This argument is not found to be fully persuasive.

Applicant only enables isolation of a raffinose synthase from *Vicia faba* legume.

Applicant has not provided evidence of raffinose synthase activity of the amino acid sequence of SEQ ID NO: 3 from soybean. In addition, it is clear from the teachings of the art at the time of Applicant's invention that one of skill in the art cannot assume that based of a method of making and the amino acid sequence encoded by an isolated nucleic acid that said isolated nucleic acid encodes a raffinose synthase enzyme.

Applicant argues that even if the genus of plants is large, it would not cause the skilled artisan undue experimentation to screen the genus via PCR (page 31, 2nd paragraph of the Remarks). This argument is not found to be persuasive because of the reasons given above. One of skill in the art cannot predictably isolate other nucleic acids encoding raffinose synthase given Applicant's limited guidance, the nature of the invention and the state of the art at the time of Applicant's invention.

Double Patenting

10. Claims 1, 4, 7 and 30-36 remain and claim 45 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 16-22 and 28-30 of copending Application No. 09/301,766. This rejection is repeated for the reason of record as set forth in the last Office action mailed 26 August 2003. Applicant's arguments filed 25 February 2004 have been fully considered but they are not persuasive.

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Applicant states that they traverse this rejection but Applicant does not specifically put forth any reasoning for the traversal (page 32, 3rd paragraph of the Remarks). The rejection is herein maintained. The instant Application teaches an isolated nucleic acid isolated from soybean asserted as encoding a raffinose synthase. The copending Application teaches an isolated nucleic acid isolated from soybean, which is a partial sequence, which is asserted as encoding a raffinose synthase.

Conclusion

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR § 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Claims 6 and 43 are allowed.

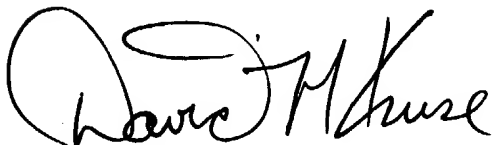
13. Claims 1, 4, 7, 9, 11-13, 15-18, 30-36, 40, 41 and 44 remain rejected and new claim 45 is rejected.

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14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David H. Kruse, Ph.D. whose telephone number is (571) 272-0799. The examiner can normally be reached on Monday to Friday from 8:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Amy Nelson can be reached at (571) 272-0804. The fax telephone number for this Group is (703) 872-9306 Before Final or (703) 872-9307 After Final.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group Receptionist whose telephone number is (571) 272-0547.



David H. Kruse
AU 1638

David H. Kruse, Ph.D.
12 May 2004